Complete Summary

GUIDELINE TITLE

The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints. London (UK): National Institute for Clinical Excellence (NICE); 2005 May. 28 p. (Technology appraisal; no. 89).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Cartilage defects in knee joints due to sporting injury, osteochondritis dissecans, or chondromalacia patellae

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Orthopedic Surgery

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assess the effectiveness and cost-effectiveness of autologous chondrocyte implantation (ACI) by examining the current evidence

TARGET POPULATION

Patients with symptomatic knee cartilage defects

INTERVENTIONS AND PRACTICES CONSIDERED

Autologous chondrocyte implantation

Note: This procedure is not recommended for the treatment of articular cartilage defects except in the context of ongoing or new clinical trials.

MAJOR OUTCOMES CONSIDERED

- Knee joint function following autologous chondrocyte implantation
- Complication rate following autologous chondrocyte implantation
- Treatment success and failure rate
- Pain
- Quality of life
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment

report for this technology appraisal was prepared by the Aberdeen Health Technology Assessment Group (see the "Companion Documents" field).

Search Strategy

Papers were identified using the following search strategies:

1. Electronic databases searched included MEDLINE (Ovid, 2000 to June 2004 for autologous chondrocyte implantation [ACI] search, 1996 to June 2004 for search of other techniques for repairing cartilage defects, and for economic search, 1966 to June 2004 for quality of life search), EMBASE (Ovid, 2000 to June 2004 for ACI search, 1996 to June 2004 for search of other techniques for repairing cartilage defects, and for economic search, 1980 to June 2004 for quality of life search), Sports Discus (2000 to 2004), The Cochrane Library (issue 2, 2004), National Health Service (NHS) Centre of Reviews and Dissemination Databases (May 2004), BIOSIS (2000 to 6 June 2004), EBSCO Biomedical Reference Collection (6 June 2004), HSTAT (6 June 2004), Science Citation Index (6 June 2004), Social Science Citation Index (6 June 2004), Department of Health Research Findings Register ReFeR (6 June 2004). Medical Subject Headings (MeSH) and keywords encompassing cartilage diseases, chondrocytes, knee diseases, knee injury, costs, quality of life, autologous implantation, and other repair techniques were sought. Details of the search strategies used are shown in appendix 3 of the systematic review companion document.
2. Databases of ongoing trials: www.controlled-trials.com (June 2004), National Research Register (6 June 2004).
3. Abstracts from the meetings of the American Academy of Orthopaedic Surgeons (2000-2004) were searched.
4. Broad internet searches were performed using a metasearch engine (Dogpile).
5. Reference lists of relevant studies and reviews identified were scanned, as well as studies reported in industry submissions to the National Institute for Health and Clinical Excellence (NICE).

Inclusion and Exclusion Criteria

Studies were included if they were prospective controlled trials (randomised controlled trials or controlled clinical trials) of ACI for localised defects of the knee, in comparison to any other or no treatment, in any patient group. Abstracts were included, provided that relevant data were shown and that publication of the abstract was not superseded by publication as a full paper. Long term (follow-up of at least two years) uncontrolled studies of interventions for localised knee defects - or natural history - were also included to enable a comparison of long term outcomes across studies. Studies in all languages were included.

Data Extraction

Two reviewers extracted data regarding study design and characteristics, details of the intervention, and patient characteristics and outcomes into a specially designed form, which was piloted before use. Differences in data extraction were resolved by discussion, referring back to the original paper. Data extraction for German studies was done by one reviewer only.

Quality Assessment

To assess the quality of controlled trials, the following criteria were assessed: 1. Method of randomisation, 2. Allocation concealment, 3. Handling of missing data/complete description of losses to follow-up, 4. Intention-to-treat analysis, 5. Power calculation, 6. Blinding of patients (if possible), 7. Blinding of carers, 8. Blinding of outcome assessors, 9. Comparable timing of outcome assessment between groups, 10. Comparable post-operative rehabilitation between groups, 11. Specification of eligibility criteria, 12. Similarity at baseline with respect to prognostic factors, 13. Presentation of point estimates and measure of variability for primary outcome measure, 14. Sponsoring by manufacturer.

NUMBER OF SOURCE DOCUMENTS

Four randomised controlled trials were included, as well as long term observational data from selected case series.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Overall study quality was rated as follows:

A. All quality criteria met
B. One or more of the quality criteria only partially met
C. One or more criteria not met

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Literature Search

The literature search undertaken by the Assessment Group identified a number of published economic studies of autologous chondrocyte implantation (ACI), although the available data appeared limited. In addition, Verigen UK Ltd submitted unpublished cost-effectiveness data in confidence. The Assessment Group undertook some illustrative modeling, comparing ACI with mosaicplasty and microfracture for patients previously treated with lavage and debridement.

Cost-Effectiveness Summary

The data on the relative effectiveness of autologous chondrocyte implantation (ACI) compared with microfracture and the still relatively experimental mosaicplasty technique were inconsistent. Furthermore, there was a lack of long-term follow-up, and the quality of life gain from treating with ACI compared with other alternatives remained unclear.

Details of the cost analysis are found in section 4.2 of the original guideline document.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Autologous chondrocyte implantation (ACI) is not recommended for the treatment of articular cartilage defects of the knee joint except in the context of ongoing or new clinical studies that are designed to generate robust and relevant outcome data, including the measurement of health-related quality of life and long-term follow-up. Patients should be fully informed of the uncertainties about the long-term effectiveness and the potential adverse effects of this procedure.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of autologous chondrocyte implantation (ACI) for the treatment of articular cartilage defects of the knee joint

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- The trials published in the literature thus far all compare autologous chondrocyte implantation (ACI) with a different treatment. Therefore, data on each comparison are limited and no trial data are available for comparing ACI with no treatment. Follow-up from the trials so far has only been up to two years, with longer-term outcomes being uncertain.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- National Health Service (NHS) hospitals and clinicians who care for people who have articular cartilage defects of the knee joint should review their current practice and policies to take account of the guidance set out in Section 1 of the original guideline document and in the "Major Recommendations" section of this summary.

- Autologous chondrocyte implantation (ACI) should be performed only within the context of ongoing or new clinical studies that are designed to generate robust and relevant outcome data. Patients should be fully informed of the uncertainties about the long-term effectiveness and the potential adverse effects of this procedure.

IMPLEMENTATION TOOLS

Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints. London (UK): National Institute for Clinical Excellence (NICE); 2005 May. 28 p. (Technology appraisal; no. 89).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Dec (revised 2005 May)

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Appraisal Committee Members: Ms Julie Acred, Chief Executive, Derby Hospitals, Southern Derbyshire Acute Hospitals NHS Trust; Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Professor David Barnett, Professor of Clinical Pharmacology, University of Leicester; Dr Peter Barry, Consultant in Paediatric Intensive Care, Leicester Royal Infirmary; Mr Brian Buckley, Vice Chairman, InContact; Professor Mike Campbell, Statistician, Institute of General Practice & Primary Care, Sheffield; Dr Mark Chakravarty, Head of Government Affairs and NHS Policy, Procter and Gamble Pharmaceuticals (UK) Ltd, Egham, Surrey; Dr Peter I Clark, Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Wirral, Merseyside; Ms Donna Covey, Chief Executive, National Asthma Campaign; Dr Mike Davies, Consultant Physician, University Department of Medicine & Metabolism, Manchester Royal Infirmary; Professor Jack Dowie, Health Economist, London School of Hygiene; Professor Gary A Ford (Vice Chair) Professor of Pharmacology of Old Age/Consultant Physician, Newcastle upon Tyne Hospitals NHS Trust; Dr Fergus Gleeson, Consultant Radiologist, The Churchill Hospital, Oxford; Ms Sally Gooch, Director of Nursing, Mid Essex Hospital Services Trust; Professor Trisha Greenhalgh, Professor of Primary Health Care, University College London; Miss Linda Hands, Clinical Reader in Surgery, University of Oxford; Professor Robert Kerwin, Professor of Psychiatry and Clinical Pharmacology, Institute of Psychiatry, London; Ms Joy Leavesley, Senior Clinical Governance Manager, Guy's and St Thomas' NHS Trust; Ms Rachel Lewis, Staff Nurse (Nephrology), Hull Royal Infirmary; Professor Jonathan Michaels, Professor of Vascular Surgery, University of Sheffield; Dr Ruairidh Milne, Senior Lecturer in Public Health, National Coordinating Centre for Health Technology Assessment, University of Southampton; Dr Neil Milner, General Medical Practitioner, Sheffield; Dr Rubin Minhas, General Practitioner with a Special Interest in Coronary Heart Disease, Primary Care CHD Lead, Medway PCT & Swale PCT; Mr Richard Devereaux-Phillips, Public Affairs Manager, Medtronic Ltd; Professor Mark Sculpher, Professor of Health Economics, Centre for Health Economics, University of York; Dr Ken Stein, Senior Lecturer, Peninsula Technology Assessment Group (PenTAG), University of Exeter; Professor Andrew Stevens (Chair) Professor of Public Health, University of Birmingham; Mr Miles Scott, Chief Executive, Harrogate Health Care NHS Trust

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The use of autologous chondrocyte implantation (ACI) for the treatment of cartilage defects in knee joints. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 2 p. (Technology appraisal 89). Available in Portable Document Format (PDF) from the National Institute for Clinical Excellence (NICE) Web site.
- Clinical and cost-effectiveness of autologous chondrocyte implantation for cartilage defects in knee joints; technology assessment report. Aberdeen (UK): Aberdeen Health Technology Assessment Group; 2004 Aug. 101 p. (Technology appraisal 89). Available in Portable Document Format (PDF) from the National Institute for Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N870. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Autologous chondrocyte implantation (ACI) for treating cartilage damage in the knee. Understanding NICE guidance - information for people with cartilage damage in the knee, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 7 p.

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0871. 11 Strand, London, WC2N 5HR.

NGC STATUS

This summary was completed by ECRI on November 29, 2005.

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